

542,684

Rec'd. CTMPC 19 JUL 2005

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
19 August 2004 (19.08.2004)

PCT

(10) International Publication Number
WO 2004/069773 A1

(51) International Patent Classification⁷: C07B 59/00,
C07K 5/00, C12Q 1/00, G01N 33/534, C07C 237/22

(21) International Application Number:
PCT/CA2004/000152

(22) International Filing Date: 5 February 2004 (05.02.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/445,560 7 February 2003 (07.02.2003) US

(71) Applicant (for all designated States except US):
MERCK FROSST CANADA & CO. [CA/CA]; 16711
Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): COLUCCI, John
[CA/CA]; 16711 Trans-Canada Highway, Kirkland,
Québec H9H 3L1 (CA). GIROUX, Andre [CA/CA];

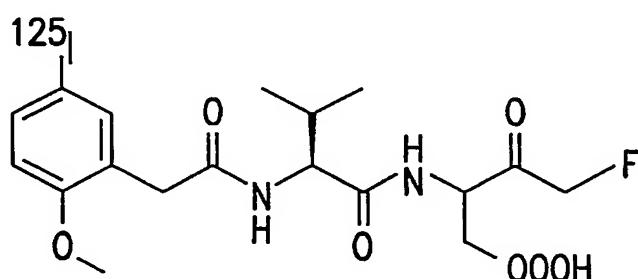
16711 Trans-Canada Highway, Kirkland, Québec H9H
3L1 (CA). HAN, Yongxin [CA/CA]; 16711 Trans-Canada
Highway, Kirkland, Québec H9H 3L1 (CA). METHOT,
Nathalie [CA/CA]; 16711 Trans-Canada Highway, Kirk-
land, Québec H9H 3L1 (CA). NICHOLSON, Donald,
W. [CA/CA]; 16711 Trans-Canada Highway, Kirkland,
Québec H9H 3L1 (CA). ROY, Sophie [CA/CA]; 16711
Trans-Canada Highway, Kirkland, Québec H9H 3L1
(CA). VAILLANCOURT, John, Paul [CA/CA]; 16711
Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA).
TAWA, Paul [CA/CA]; 16711 Trans-Canada Highway,
Kirkland, Québec H9H 3L1 (CA).

(74) Agent: OGILVY RENAULT; Suite 1600, 1981 McGill
College Avenue, Montreal, Québec H3A 2Y3 (CA).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

[Continued on next page]

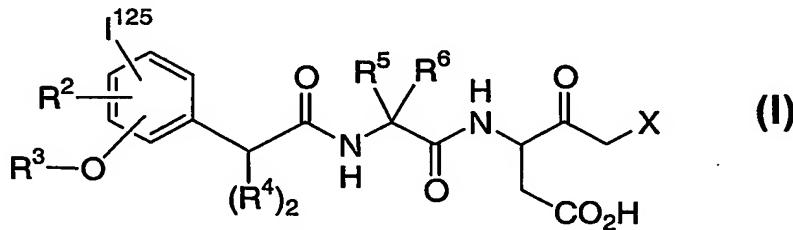
(54) Title: IRREVERSIBLE CASPASE-3 INHIBITORS AS ACTIVE SITE PROBES



$k_{inact} (S^{-1})$

CASPASE-1	7.0×10^{-6}
CASPASE-3	1.6×10^{-5}
CASPASE-7	1.2×10^{-6}
CASPASE-8	3.7×10^{-5}

[¹²⁵I]-M808



WO 2004/069773 A1

(57) Abstract: The present invention encompasses a compound of Formula (I) useful as caspase active site probes. These probes can be used to determine whether a caspase has been activated, in cells or in tissues of animal models of various pathologies. Furthermore, through competition based assays, these caspase active site probes can be used to calculate the percentage of occupancy of active caspases by other, unlabeled inhibitors.



PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.